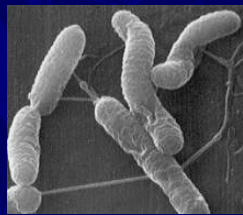
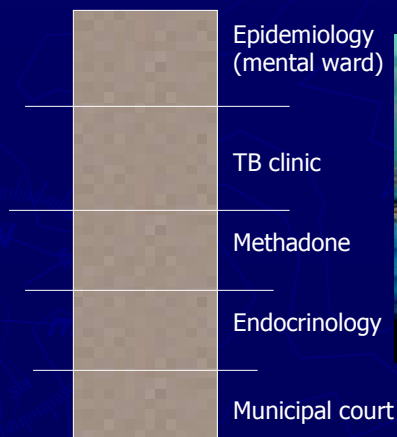


# *Helicobacter pylori* in Northern California

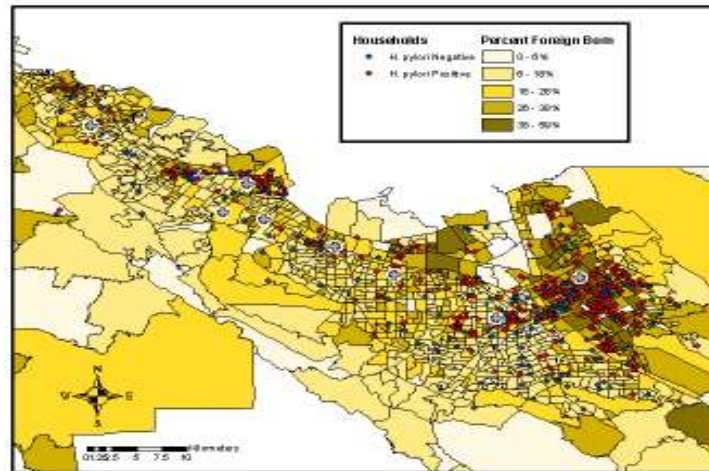


Sharon Perry  
Stanford University  
July 31, 2009

## Elevator, Bldg 90 San Francisco General Hosp.



## Stanford Infection and Family Transmission Studies



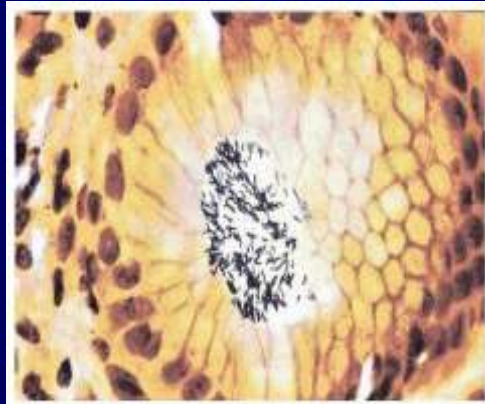
## Outline

- ▶ Epidemiology and risks
- ▶ Northern California studies of concurrent infection
  - Gastroenteritis
  - *M. tuberculosis* infection
  - New Refugee studies

## The rediscovered pathogen

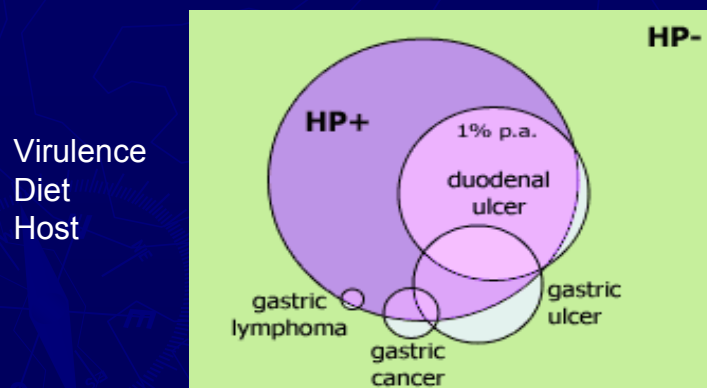


Robin Warren & Barry Marshall, 2005

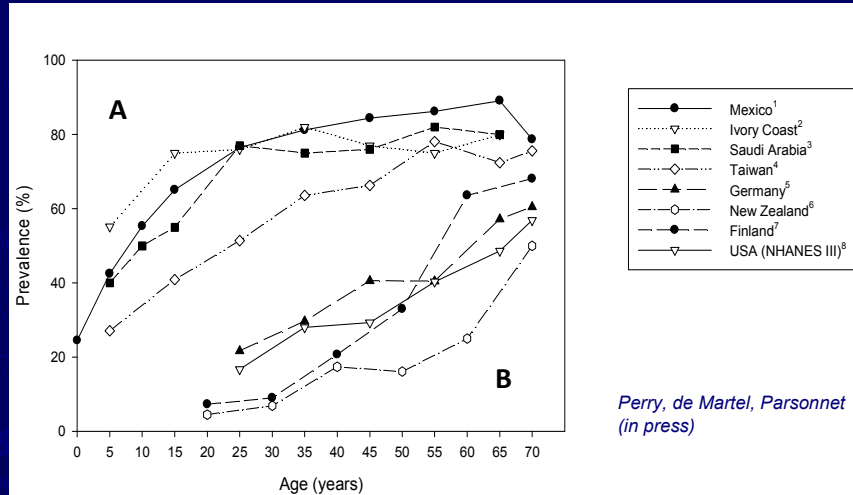


*H. pylori* in a gastric gland

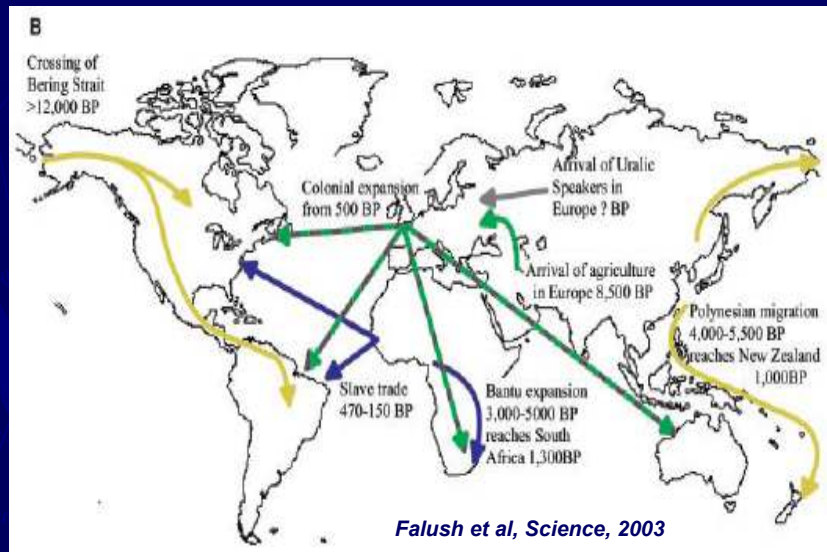
## Clinical outcomes of *H. pylori* infection



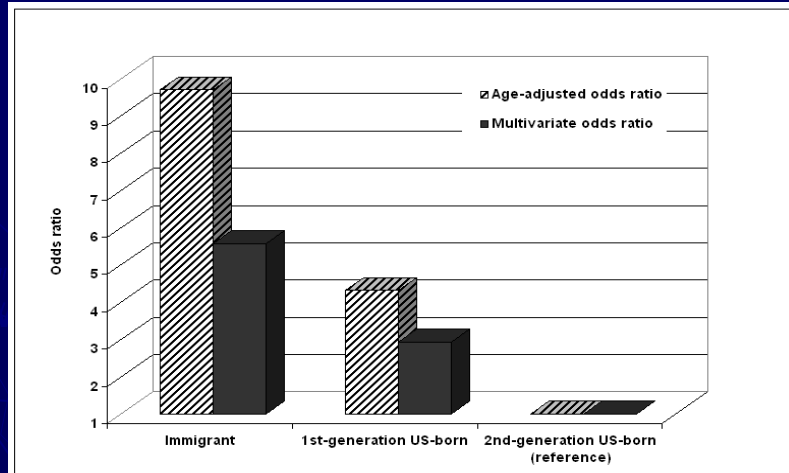
# Age of acquisition



## Ancient and intimate

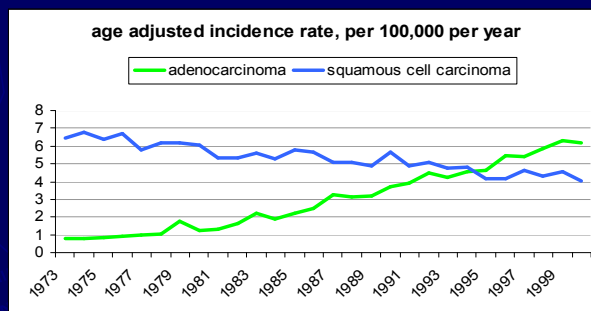


## Disappearing



*Tsai et al, AJE, 2005*

## Secular trends: esophageal cancer



SEER registry, 2003

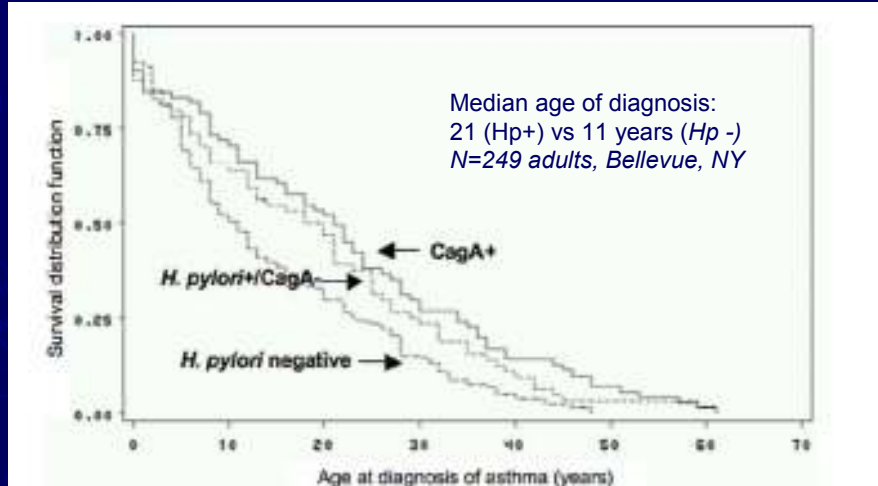
White men, US

<i>H. pylori</i>	Adjusted Odds (95% CI)*
Seronegative	1.0
Seropositive	0.37 (0.16-0.88)

De Martel et al, 2006  
Kaiser-No. California

\*BMI, smoking, education

## Secular trends: asthma



Reibman et al, 2008 (PLOS ONE)

## Old world triad

	<i>H. pylori</i>	<i>M. tuberculosis</i>	Intestinal Helminthiasis
Global prevalence	>50%	>30%	>30%
Clinical Outcome (%)	Ulcer (20) Cancer (<3)	TB (10)	multiple (15)
Immune Response			
Humoral	Strong	Weak	Strong
Cellular	Th1-like	Th1-like	Th2-like

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# What about the other 80%?

Chronic infections  
may persist because  
they provide  
survival advantage

--*Charles Darwin*



## Study Designs

### Incidence of gastroenteritis

*Family studies*

2 home visits

*H. pylori IgG, Stool testing*

### Rates of coinfection IFN- $\gamma$ responses

*TB testing*

2 home visits

Clinic visit

*TST, QuantiFERON-TB GOLD*

## *H. pylori* reduces risk of gastroenteritis

Age-adjusted OR = 0.38 (95% CI = 0.14 – 1.0)

	HAV infected	HAV uninfected
<i>H. pylori</i> infected	0.4 (0.19 - 0.85)	0.25 (0.08 - 0.82)
<i>H. pylori</i> uninfected	0.46 (0.24 - 0.88)	1.0

Perry et al, 2006

*p for interaction=0.05*

## Herpesvirus latency confers symbiotic protection from bacterial infection

### AMERICAN REVIEW OF RESPIRATORY DISEASE

*and Laboratory Studies of Tuberculosis and Respiratory Disease*

March 1968

#### FIFTIETH ANNIVERSARY EDITORIAL

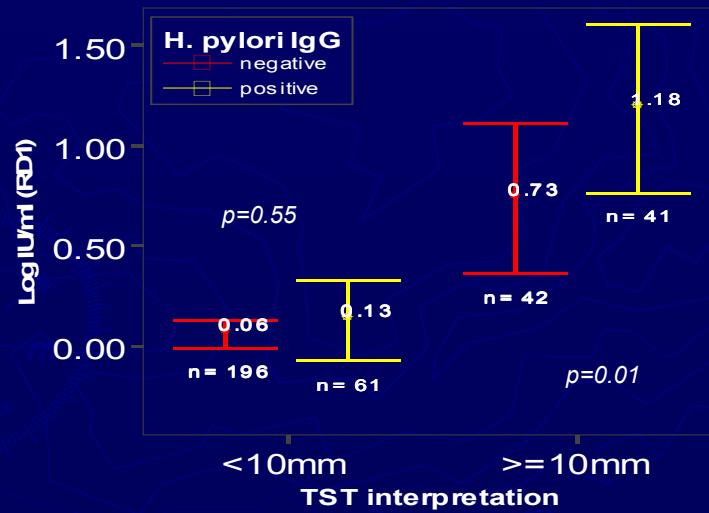
*g represents the sixth of a series of Editorials that will appear in the Fiftieth Anniversary of the Review. Each writer has been invited to write about some aspect of respiratory disease that is very much on his mind at the time.*

THE

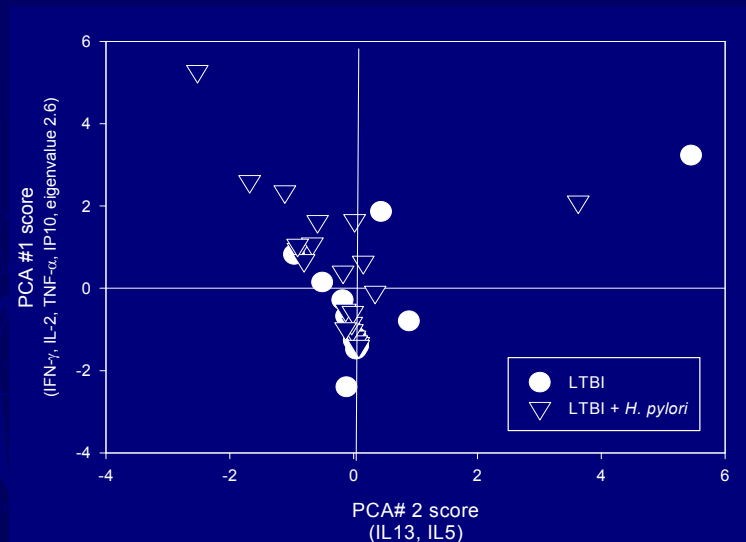
**The Immunology of Antituberculous Immunity**



## *H. pylori* and enhanced IFN- $\gamma$ responses to specific TB antigens



## ... and enhanced Th-1 like cytokine profile



## Hypothesis

- ▶ *H. pylori* coinfection promotes control of *M. tuberculosis* infection
- ▶ Helminth co-infection interferes with adaptive immune responses to both
- ▶ *These differences may be tested by comparing coinfecting individuals before and after treatment for LTBI or helminth infections*

## Refugee studies

In the long history of humankind  
(and animal kind, too) ...

those who learned to  
collaborate and  
improvise most effectively have  
prevailed

--Charles Darwin



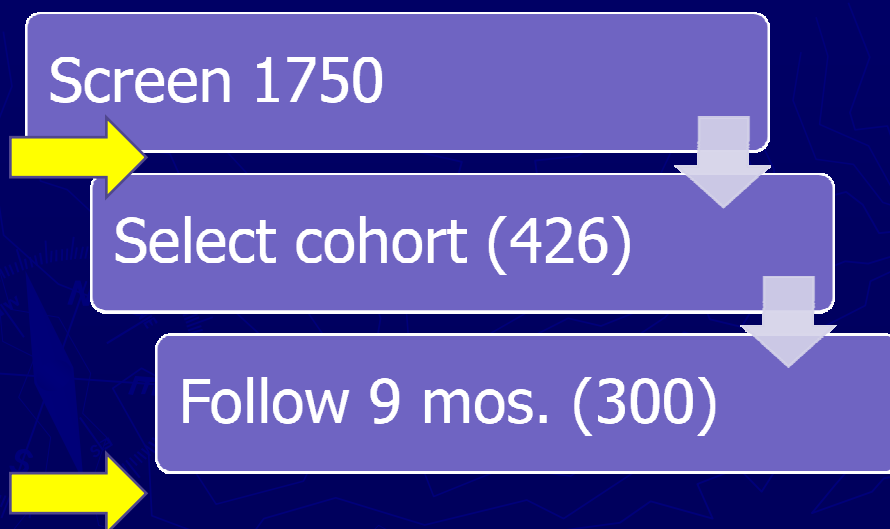
Event: Relief for San Francisco Earthquake  
Date: 18 April 1906

## Study Aims

- ▶ Characterize joint distribution of *H. pylori*, latent tuberculosis, and intestinal helminth infections in recent immigrants to Northern California
- ▶ Measure immune responses to **co-infection**
  - before and after treatment of LTBI or helminth infection

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## Study Design



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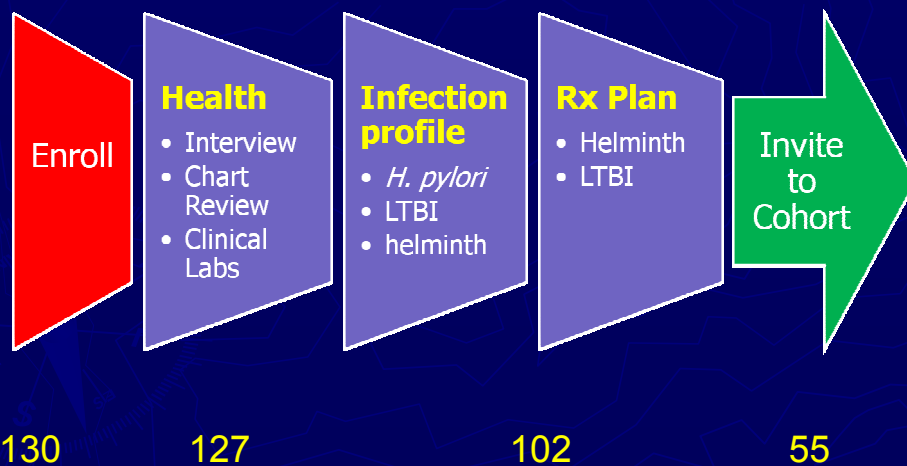
*Analysis: End of study compares samples banked at 2 time points*

## Target population

- Adults 18-45 yrs
- Recent immigrant/endemic country (<2 yrs US)
- Receiving TST/IGRA (screening indication)
  - No Hx treatment for TB or LTBI
- Asymptomatic
- “Clinically well”
- Female: not pregnant or lactating

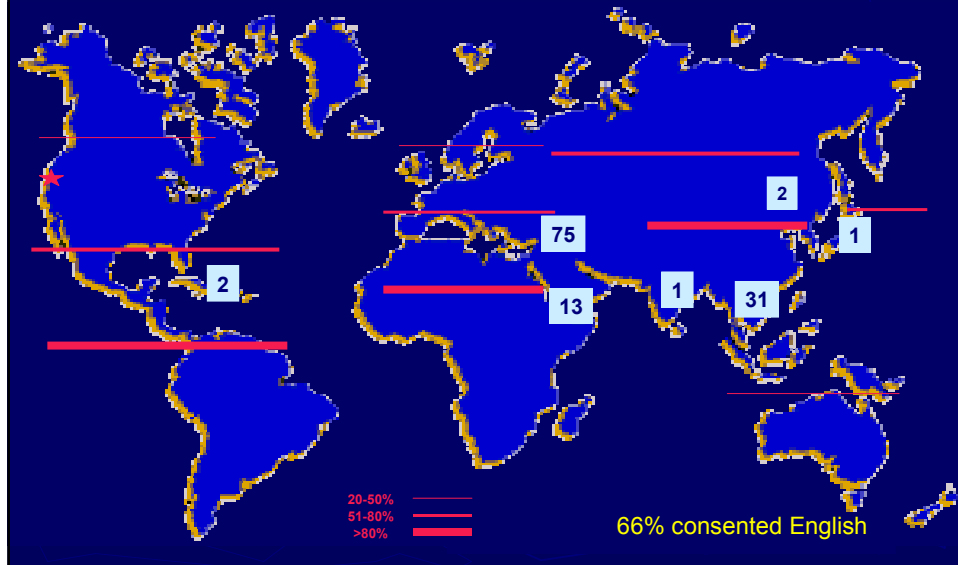
23

## Santa Clara Cty TB/Refugee collaboration



24

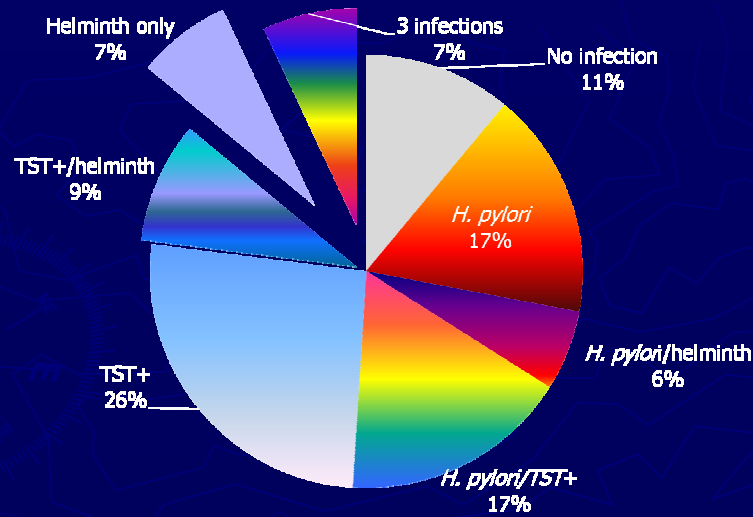
## Where are they from?



## Prevalence of infections

Test	# done	Positive
<i>H. pylori</i> infection (sero)	117	59 (50%)
Latent TB infection		
TST $\geq 10$	115	68 (59%)
QFT $\geq 0.35$ IU/ml	117	18 (15%)
Helminth infections		
O/P (other patho)	103	2 (15 other patho)
<i>S. stercoralis</i> (sero)	112	29 (26%)
Cysticercosis (sero)	106	3 (3%)
Schistosomiasis spp (sero)	106	10 (9%)

## Patterns of infection



## Companion studies back home

A.

B.

## ***Odds of *H. pylori* infection in TB cases and household contacts***

*TB Outcome*

Adjusted Odds (95% CI)

Nonprogressor

1.0

Prevalent TB case

0.55 (0.36-0.83)

New TB case

1.4 (0.65-3.0)

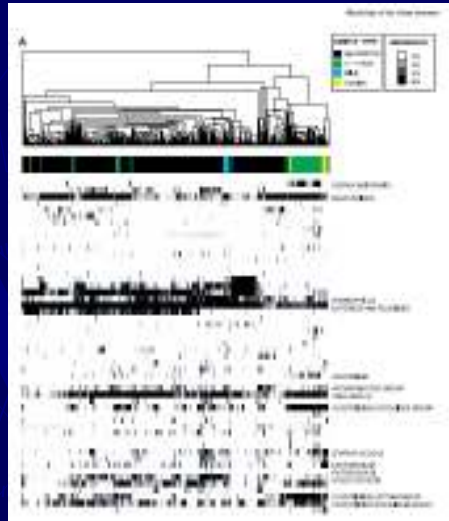
LTBI @ baseline  
19 (68%)

LTBI @ baseline  
262 (64%)

LTBI @ baseline  
7 (88%)

LTBI @ baseline  
70 (75%)

# Human microbiome



- ▶ 1<sup>st</sup> year of life
- ▶ In adults, ratio of microbial to human cells 10:1
- ▶  $10^{12}$  microbes/ml lumen in the intestine

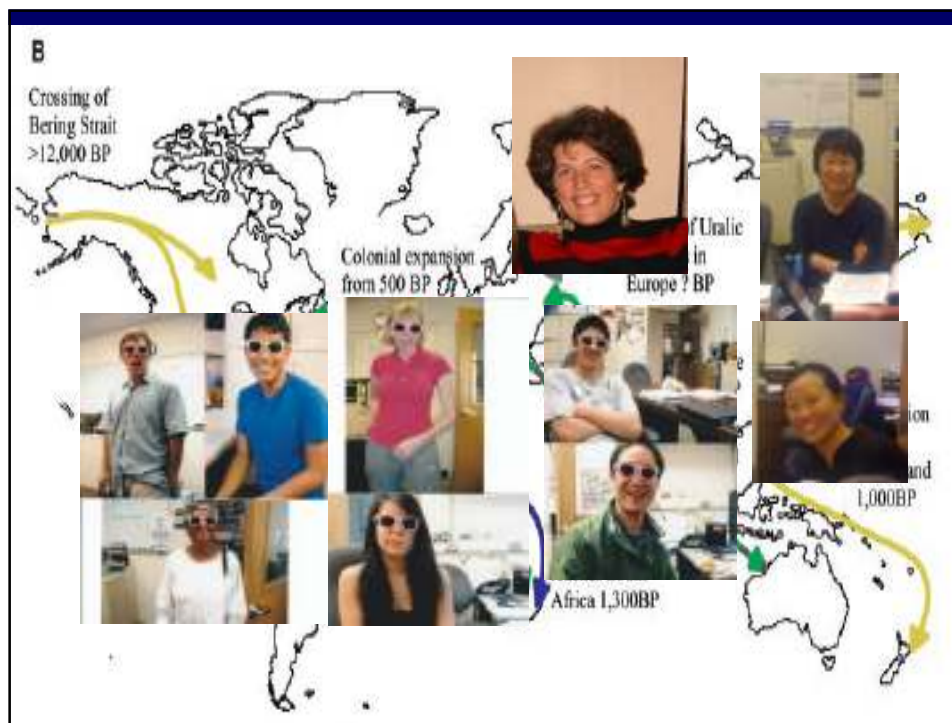
*Palmer et al, PLOS Biology, 2007*

## Summary

- ▶ *H. pylori* an important marker of epidemiologic transitions
- ▶ Co-infection is common in recent US immigrants
  - There may be benefits as well as risks to asymptomatic infection
- ▶ What about the other 80%?
  - Human microbial ecosystem plays an important role in protection from specific infections

## The new world

*"...[O]nce we understand nature's transformative powers, we see that it is our powerful ally, not a force to be feared or subdued."*  
--Thomas Kuhn





## QFT/TST agreement

Adults			
	QFT+ ( $\geq 0.35$ IU/ml)	QFT- ( $< 0.35$ IU/ml)	Total
TST $\geq 10$ mm	22	23	45
TST $< 10$ mm	11	152	163
Total	33	175	208
<i>Kappa= 0.49 (0.31-0.62)</i>			

48%

Children			
	QFT+ ( $\geq 0.35$ IU/ml)	QFT- ( $< 0.35$ IU/ml)	Total
TST $\geq 10$ mm	3	16	19
TST $< 10$ mm	4	88	92
Total	7	104	111
<i>Kappa= 0.15 (-0.07-0.38)</i>			

16%

## QFT/TST calibration

